UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/083,861	02/25/2002	Ram I. Mahato	T8948.CIP	5816

7590 04/07/2004

M. Wayne Western
THORPE, NORTH & WESTERN, L.L.P.
P.O. Box 1219
Sandy, UT 84091-1219

EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,861	MAHATO ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *01 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/1/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Application is a CIP of prior Application 09/662,511, filed 9/14/2000, now US Patent 6,696,038.

An information disclosure statement was received on 5/1/02.

Claims 1-35 are pending and under consideration in this Office Action.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because:

-it states that the specification that was reviewed and understood by the inventors was that of Application 09/662,511, and because

-it fails to acknowledge the duty to disclose prior art that may have become available between the filing dates of the parent and instant applications.

The instant application is a continuation in part of 09/662,511, and has been amended. See e.g. paragraph 42, which was not contained in the parent application. A new oath or declaration is required which correctly identifies the specification that was reviewed and understood, and which acknowledges the duty to disclose all information known to the person to be material to patentability which became available between the filing date of the prior application and the filing date of the continuation-in-part application. See 37 CFR 1.56(e).

Specification

The specification is objected to because the priority document, US Application 09/662,511, has issued as US Patent 6696038 B1. The first line of the specification should be amended to reflect this fact. Also, the specification discloses at paragraph 78 "[Table 1]". No table accompanies this passage. Although, the "Table 1" appears in brackets, no amendment directing deletion of any table or text ahs been received by the Office. Clarification is requested.

Compliance with Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s). This application clearly fails to comply with the requirements of 37 C.F.R.1.821-1.825. Applicant's attention is directed to the final rule making notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998). **The specification at page paragraph 92 discloses oligonucleotide sequences in excess of 10 bases amino acids that are not accompanied by a SEQ ID NO.** If these sequences are listed in the current Sequence Listing, then the specification should be amended to include the appropriate SEQ ID NOS in the

passage referred to above. If these sequences are not in the current Sequence Listing, then Applicant must provide:

A substitute computer readable form (CRF) copy of the "Sequence Listing".

A substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

PatentIn Software Program Support

Technical Assistance.....703-287-0200

To Purchase PatentIn Software.....703-306-2600

Claim Objections

Claims 1, 8, 15, 22, and 34 are objected to because the phrase "cholesterol derived" should be hyphenated.

Claims 1, 8, 15, 22, and 34 are objected to because they lack a space between "polyethylenimine" and "(PEI)".

Claims 4, 11, 19, and 25 are objected to because they lack a space between "polyethylene glycol" and "(PEG)".

Claims 5, 12, 20, and 26 are objected to because "stemcell" should be two words, i.e. "stem cell", and because they contain the conjunction "and" prior to the penultimate member of the recited Markush group. More specifically, "and" is inserted after the words Lewis^X, and "lactose". In the recited Markush format, i.e. "selected from the group consisting of ...", the conjunction "and" should separate only the penultimate and last recited species.

Claims 5, 12, 20, and 26 are objected to because hemagglutinin is misspelled as "hemaglutinin".

Claims 6, 13, 21 and 27 are objected to because galactose is misspelled as "galctose".

Claims 7, 14, 16, and 28 are objected to because they lack an article prior to the noun "molar ratio".

Claims 8, 15, 22, and 34 are objected to because they lack an article prior to the noun "biocompatible hydrophilic polymer spacer".

Claim 32 is objected to because it lacks a space between "dioleoylphosphatidylethanolamine" and "(DOPE)", and it lacks a space between "oleoylpalmitoyl-phosphatidylethanolamin" and "(POPE)". Also, "oleoylpalmitoyl-phosphatidylethanolamin" and "diphytanoylphosphatidylethanolamin" are misspelled. Both of these words should end in "e".

Claims 34 and 35 are objected to because they recite "a effective" rather than "an effective".

Claim 29 is objected to because it lacks a comma after "protein".

Claim 32 is objected to because distearoyl is misspelled as "disteroyl".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-35 are indefinite because they recite "the cholesterol derived lipid anchor without antecedent basis.

Claims 1-35 are indefinite because they are ambiguous as to the structure of the claimed compound. Specifically, these claims require a linker that covalently links three entities, an anchor lipid, PEI, and a spacer. The simplest interpretation of the claims is that the linker must form a covalent bond to each of the three entities, i.e. three different covalent bonds, one to each entity. However, claims 2, 9, 17, and 23 require that the linker must be an ester bond. One of ordinary skill in the art appreciates that an ester linkage can be formed between only two entities, not three, thus the nature of the claimed structure is unclear.

Claims 1-35 are indefinite because it is unclear what is intended by "non-toxic". The specification fails to define this term, and sets forth no standard with which comparison may be made. For example, "non-toxic" could be used to describe effects

on a cellular level, or alternatively, on the level of the whole organism. For this reason, one of skill in the art cannot know the metes and bounds of the claims.

Claims 2, 9, 17, and 23 are also indefinite because they require that the claimed linker must be "an ester bond". In essence, the linker is required to be a pair of electrons, i.e. a single bond. Generally, as a term of art, the term "linker" refers to molecules or functional groups comprising at least two bonds, i.e. one bond between the linker and the first linked group, and another separate bond between the linker and the second linked group. The term is not generally used to refer to only a single bond. For example, the specification teaches at paragraph 39 that carbamate, urea, amide, and amine groups are considered to be linkers. It is suggested that the term "linkage", or the term "group", should be substituted for the word "bond".

Claim 3 is indefinite because it recites "its derivative" without proper antecedent basis. The use of the singular form "derivative" implies that there is only a single derivative of cholesterol, and that this single derivative is what is claimed. In fact cholesterol has many derivatives, so one of skill in the art cannot know to which of these derivatives Applicant refers.

Claims 4, 19, and 25 are indefinite because it is unclear what is intended by the phrase "between 0.5 to 20K Daltons". The phrase "0.5 to 20K Daltons" describes a finite range of molecular weights. While it is conceivable for an object to be *within* a range of molecular weights, it does not make sense to require that an object must be *between* a range. It is similar to requiring that a number must be "between an integer".

Substitution of the word "and" for the word "to" in the phrase "0.5 to 20K Daltons" is suggested.

Claims 7, 14, 16, and 28 are indefinite because they recite the phrase "preferably within a range of". This phrase renders the claims indefinite because it is it is not clear whether the recited range is a limitation, or not, i.e. it is unclear whether or not the scope of the invention is further limited by the claim.

Claims 10, 18, and 24 are indefinite because it is unclear to what "a derivative thereof" refers. It is unclear if the derivative is intended to be a derivative only of a "C_{12} to C_{18} fatty acid", or if it may also be a derivative of "a cholesterol".

Claim 32 is indefinite because it is unclear what is intended by "disteroyl-, -palmitoyl-, -myristoylphosphatidylethanolamine". If Applicant intends distearoylphosphatidylethanolamine, dipalmitoylphosphatidylethanolamine, and dimyristoylphosphatidylethanolamine, then the claim should be redrafted accordingly.

Claim 32 is also indefinite because it is unclear to what "1- to 3-fold N-methylated derivatives thereof" refers. It is unclear if the derivatives are intended to be a derivatives only of "disteroyl-, -palmitoyl-, -myristoylphosphatidylethanolamine", or if they may also be a derivatives of any of the other lipids recited in the Markush group.

Claims 34 and 35 are indefinite because they recite "the composition" without antecedent basis.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to the genus of biodegradable lipopolymers comprising four elements including a links a lipid anchor, a branched polyethyleneimine, a biocompatible hydrophilic polymer spacer, and a biodegradable linker. The only information in the claims regarding the structural organization of these elements is that the linker must covalently link the other three elements. As discussed above, under 35 USC 112, second paragraph rejections, the intended scope of the claims is unclear because the structural organization is not clear. Although the claims require a linker that covalently links the other three species, the specification does not appear to contemplate such a species, i.e. one in which a single linker forms three covalent bonds, one to each of the other three recited elements. In fact, the specification contemplates only two species of lipopolymer that comprise the four recited structural elements, but neither of these lipopolymers meets the claim limitation in which the linker covalently links the other three elements. At paragraph 42, the specification teaches a species in which a lipid anchor is connected to branched PEI by a hydrophilic polymer spacer (e.g. PEG), but paragraph 42 does not teach the location of any linker in this species. However, at example 14, it is clear that the linker is present and joins the lipid

anchor and PEG. PEI is then covalently attached to PEG, but not through the use of the linker. The specification also teaches at paragraph 43 a composition in which a lipid anchor is connected to branched PEI, and a targeting moiety is attached to PEI by a spacer. Paragraph 43 does not teach the location of any linker, but the specification teaches generally that when a lipid anchor is joined to PEI, this is accomplished by a linker. So this species can be considered to be organized as: lipid anchor-linker-PEI-spacer-targeting ligand. Again the linker joins only two of the three elements covalently. These are the only two combinations of the four recited elements that the specification can be considered to contemplate. Furthermore, claim 2 for example requires that the linker must be an ester bond. It is clear to one of ordinary skill in the art that three different molecules cannot be joined by a single ester bond.

At the time the invention was filed it was routine to link a lipid anchor to PEI by means of an ester linkage (see Epand et al (US Patent 5,283,185)). However, there is no evidence of record that it was routine in the art at the time of the invention to use a single linker to covalently join a lipid anchor, a polycation, and a spacer. In view of the state of the prior art and Applicant's disclosure, one of skill in the art could not conclude that Applicant was in possession at the time of the invention of any combination of the four recited elements, other than those that were clearly contemplated, and it is clear that Applicant was not in possession of a composition in which a linker forms three covalent bonds, one to each of the other three elements. The specification can be considered to adequately describe only the two species disclosed in paragraphs 42 and

43 as discussed above. Applicant is encouraged to limit the claims to these species, as they are free of the prior art of record.

Claims 1-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a biodegradable non-toxic cationic lipopolymer comprising a branched chain PEI, a lipid anchor, a biocompatible hydrophilic polymer spacer, and a biodegradable linker, wherein the PEI is covalently linked to the lipid anchor by the linker, and the polymer spacer is covalently attached to PEI at one end, and to a targeting ligand at the other end, and while enabling for a biodegradable non-toxic cationic lipopolymer comprising a branched chain PEI, a lipid anchor, a biocompatible hydrophilic polymer spacer, and a biodegradable linker wherein the lipid anchor is covalently linked to one end of the polymer spacer via the linker, and the PEI is covalently attached to the other end of the spacer, does not reasonably provide enablement for any other arrangement of these four structural elements into a biodegradable non-toxic lipopolymer, particularly one in which a single linker forms covalent bonds with each of the three other structural elements of the lipopolymer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

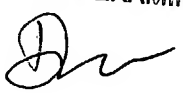
As discussed above, the specification fails to describe any arrangement of the four structural elements of the lipopolymer than those set forth in the statement of the rejection. Thus, the specification fails to provide the essential guidance that is

necessary to make any other lipopolymer that is embraced by the claims. While Applicant is not required to disclose that which is well known in the art, there is an obligation to disclose critical elements of the invention as well as how to use these elements. In Genentech, Inc, v Novo Nordisk A/S, the court found that when the specification omits any specific starting material required to practice an invention, or the conditions under which a process can be carried out, there is a failure to meet the enablement requirement. See 42 USPQ2d 1001.

> It is true, as Genentech argues, that a specification need not disclose what is well known in the art. See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

In this case, the identification of a linker that covalently attaches to each of a lipid anchor, PEI, and a spacer, as well as the other conceivable structural arrangements of the four recited structural elements cannot be considered to be minor details that can be omitted in the process of presenting an enabling disclosure. As such one of skill in the art would have to perform undue experimentation in order to make lipopolymers other than those discussed above.

DAVE T. NGUYEN
PRIMARY EXAMINER



Conclusion

No claim is allowed. All claims are free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 571-272-0564.

Richard Schnizer, Ph.D.